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Biochemical Assessment of Pregnancy-Related Physiological Changes in Renal Function

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Abstract

This study was aimed at determining biochemical markers of renal function in pregnant women in Kano State, Nigeria. Urea, electrolytes and creatinine were estimated from 45 pregnant women and 45 non pregnant apparently healthy, age-matched controls. The result of the study showed significant difference (P<0.01) in urea, creatinine and bicarbonate levels between the pregnant and non- pregnant women but no significant difference (p>0.01) was observed in sodium, potassium and chloride levels between the two groups. Studies within the trimesters showed significant difference (p<0.05) in urea levels between the control group of the 1st and 2nd trimesters.

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Creatinine levels in the 2nd trimester (43.20±12.3) and 3rd trimester (41.40±5.45) were found to be significantly lower ($p<0.05$) compared to the control group (55.84±16.17). A significant difference in creatinine levels ($p<0.05$) between the 1st and 2nd and the 1st and 3rd trimesters was also recorded. The mean difference in bicarbonate levels in the 1st (22.33±1.84), 2nd (21.80±1.37) and 3rd(21.73±1.79) trimesters and the -

control group (26.09±2.08) was significantly lower ($p<0.05$) with no significant difference within the trimesters. There was no significant difference ($p>0.05$) observed in sodium, potassium and chloride level between the control groups and the trimesters of pregnancy. The result obtained is indicative of normal renal function in the study groups.

Keywords: Renal function; Pregnancy; Urea; Electrolytes; Creatinine.

1. Introduction

Pregnancy is a normal psychological phenomenon with many biochemical changes (ranging from alterations in fluid and electrolyte concentrations to more complex changes in cortisol and calcium metabolism) that assist the nurturing and survival of the fetus. Biochemical parameters reflect these changes and are clearly distinct from the non-pregnant state. It has been reported that the imbalance in metabolites depends on several factors including nutrition, genetics and mother's lifestyle [1].

The kidney undergoes tremendous anatomic and physiologic changes in pregnancy characterized by enlargement due to increase in both vascular and interstitial space albeit no accelerated growth akin to compensatory hypertrophy [2, 3]. The most marked structural change is the dilatation of the calyces, renal pelvis and ureter resulting in hydronephrosis.[r4]Hydronephrosis have been documented to occur with variable frequency (43%-100%) and a peak incidence at 28 weeks of gestation[4,5]. Kidney volume may increase by upto 30% and increase in length have been documented independent of pelviectasis [6,7]. Both hormonal and mechanical factors play a role in these structural changes the kidneys undergoes during pregnancy. This ranges from the effect of progesterone on the tone and force of contraction of the ureter to the compression effect exerted by the weight of the uterus as the pregnancy advances.

Several studies have documented the characteristic increase in GFR and hyperfilteration which tend to resolve by 4 weeks postpartum [8,9,10,11,12].The increased GFR is in part due to increase in the level of aldosterone which expands the blood volume by up to 50% and increase renal blood flow. A net fall in oncotic pressure due to volume expansion further augments filtration at the glomerulus by increasing filtration pressure.

Pregnancy is also associated with several alterations in tubular handling of filtered nutrients and waste products of metabolism. Reduced proximal tubular reabsorption of glucose coupled by increased tubular flow rate underlie the glucosuria seen in some pregnancies. The increased uric acid excretion noted in first and second trimesters of pregnancy results in a fall in serum levels. This is followed by a gradual rise in the third trimester. The significance of this is thought to be due to the need to accommodate the increased production from the placenta and fetus [13]. Decreased fractional reabsorption of amino acids and β-microglobulin result in the increased excretion of these substances [13].

Renal function test classified as glomerular and tubular function tests assess the ability of the kidney to carry out its numerous functions. Biochemical parameters routinely measured include urea, electrolyte Sodium (Na+), bicarbonate (HCO3-), chloride (Cl-), potassium (K+) and creatinine as well as albumin, total protein and uric acid.

The biochemical Changes in renal function accompanying normal pregnancies in black race of African descent is not well documented. Thus, the purpose of this study was to use biochemical markers in describing these changes in pregnant women attending ante-natal clinic at Aminu Kano Teaching Hospital (AKTH), Kano, Nigeria.

2. Materials and Methods

The study subjects included forty five (45) pregnant women and forty five (45) non pregnant apparently healthy, age-matched control subjects aged between 19-35 years (with no known history of renal problems) attending antenatal clinic at Aminu Kano Teaching Hospital (AKTH) Kano State, Nigeria. The control group consisted of forty five (45) apparently healthy, non- pregnant, age matched women selected from amongst the students of various departments of Bayero University Kano. The non- pregnant participants constituted group I. Depending on the stages of pregnancy (trimesters), the pregnant subjects were divided into three groups of 15 subjects each, designated group II (first trimester pregnant subjects), group III (second trimester pregnant subjects) and group IV (third trimester pregnant subjects.

Blood sample (5ml) was collected from all the participants (study subjects and control) by venipuncture with minimum stasis into vacutainer sample bottles (containing gel serving as clot activator). The blood was allowed to clot at room temperature and centrifuged at 3000rpm for five minutes. The serum was then transferred into plain containers and kept frozen until analysis. The serum samples were assayed for urea, electrolytes (Na^+, K^+, Cl^- HCO_3^-) and creatinine.Urea was estimated by Urease Berthelot'sReaction [14],sodium and potassium were estimated byFlame Photometry [15], bicarbonate [16] and chloride [17] by titration method. Creatinine was estimated using alkaline picrate method [18]. Data were analyzed using student's t-test (comparing between non pregnant, first, second and third trimesters). Z – Statistic was used to analyze the significance between pregnant and non- pregnant subjects. P values < 0.05 were considered significant for the t-test and p<0.01 for Z- statistics [19].

3. Results

The mean values of urea, creatinine and electrolyte levels in pregnant women at various trimesters and the non - pregnant control group are shown in table 1.

The mean value of serum urea in the three trimesters was found to be lower than that of the control (3.17±0.62). However, the third trimester recorded the highest concentration of urea (2.69±0.97) while the lowest mean value of 2.27±0.54 was observed in the second trimester and a urea level of 2.67±0.44 in the first trimester. Hence, urea levels decrease in the 1st and 2nd trimester with a slight increase in the 3rd trimester. A decrease in urea levels between the control group and the 1st and 2nd trimesters was observed to be statistically significant (P

<0.05). No significant difference was observed between the control group and the third trimester. Within the trimesters only the 1st and 2nd showed significant difference (P<0.05) in urea levels.

Table 1: Serum urea, creatinine and electrolyte levels in the non- pregnant control group and pregnant women at various trimesters .

Group/subjects	Urea (mmol/l)	Creatinine (mmol/l)	Sodium (mmol/l)	Potassium (mmol/l)	Bicarbonate (mmol/l)	Chloride (mmol/l)
Controlnon-pregnant n=45	3.17 ± 0.62	55.84 ± 16.17	135.64 ± 4.79	3.70 ± 0.36	26.09 ± 2.08	98.38 ±5.18
Pregnant 1st trimester n=15	2.67[a] ± 0.44	54.53 ± 10.07	135.33 ± 5.55	3.89 ± 0.27	22.33 ± 1.84	96.87 ± 5.13
Pregnant 2nd trimester n=15	2.27[ab] ± 0.54	43.20[ab] ± 12.31	136.67 ± 4.39	3.89 ± 0.56	21.80[a]± 1.37	96.00 ± 3.55
Pregnant 3rd trimester n=15	2.69 ± 0.97	41.46[ab] ± 5.54	137.80 ± 4.95	3.75 ± 0.51	21.73[a] ± 1.79	98.00 ± 4.31

a= significant (P<0.05) as compared to the control group

b= significant (P<0.05) as compared to the 1st trimester

The mean values of serum creatinine decreased progressively (54.53±10.07, 43.2±12.31 and 41.4±5.54) from the 1st to the 3rd trimesters as pregnancy advanced and were found to be lower than that of the control group (55.84±16.1). Compared to the control, there were significant differences (P<0.05) in creatinine levels in the 2nd and 3rd trimester only. Also, the mean difference between the 1st and 2nd, and 1st and 3rd trimesters were found to be significant (P<0.05) with no significant difference between the 2nd and 3rd trimester.

Serum sodium levels increased progressively from the 1st trimester to the third trimesters respectively (135.33±5.55, 136.67±4.39, 137.80±4.95) but no significant difference was observed between the trimesters and the control group and within the trimesters (P<0.05).

The mean value of serum potassium in the 1st and 2nd trimesters was found to be the same (3.89±0.27, 3.89±0.56). The lowest potassium level was recorded in the third trimester (3.75±0.51). Although, potassium levels in the three trimesters were slightly higher than the control group, no significant differences (P<0.05) were observed between the trimesters and the control group and within the trimesters.

Serum bicarbonate levels decreased progressively (22.33±1.84, 21.80±1.37, 21.73±1.79), from the 1st to the 3rd trimester and this decrease was found to be statistically significant (P<0.05) compared to the control

(26.09±2.08). No significant difference was observed within the trimesters.

Serum chloride levels decreased slightly from the 1st to the 2nd trimester with an increase in the 3rd trimester. No significant difference ($P<0.05$) was recorded within the trimesters and between the control group.

Table 2: Mean serum urea, creatinine and electrolyte levels in non- pregnant and pregnant women.

Group/Subject	Urea (mmol/l)	Creatinine {μmol/l)	Sodiun (mmol/l)	Potassium (mmol/l)	Bicarbonate (mmol/l	Chloride (mmol/l)
Control Non-Pregnant n=45	3.17±0.62	55.84±16.17	135.64±4.79	3.70±0.36	26.09±2.08	98.38±5.18
Pregnantn=45	2.54^{a}±0.69	48.04^{a}±10.64	136.60±4.97	3.84±0.46	21.96^{a}±1.66	96.96±4.35

a = significant ($P<0.01$) as compared to the control group

The mean values of urea, creatinine and electrolyte levels in non- pregnant and pregnant women are shown in table 2. The mean value of urea in the pregnant and non- pregnant women was found to be 2.54±0.69, and 3.17±0.62 respectively. The difference in mean was observed to be statistically significant ($P<0.01$). A significant difference ($P<0.01$) was observed in creatinine levels between the pregnant (48.04±10.64) and non-pregnant (55.84±16.17) women. Serum sodium level showed no significant difference ($P>0.01$) between the pregnant and non- pregnant participants. There was no significant difference ($P>0.01$) in potassium level between the pregnant and non- pregnant subjects.

The mean difference in bicarbonate level between the pregnant (21.96±1.66) and non- pregnant (26.09±2.08) was found to be significant ($P<0.01$). The mean difference in chloride level between the two groups showed no significant difference ($P>0.01$)

4. Discussion

This study was carried out to evaluate renal function in apparently healthy pregnant women attending ante natal clinic at Aminu Kano Teaching Hospital (AKTH) using the routinely analyzed biochemical markers (urea, electrolytes and creatinine). The decrease in urea levels in pregnancy could be attributed to the increase in glomerular filtration rate (GFR), hydration and increased anabolic rate that accompany normal pregnancy [20]. The increase in urea levels noticed in the 3rd trimester may be due to an increase in protein intake or the fact that most of these analytes fall back to normal levels at term. Studies by Sims and Krantz, [21], Davison and Noble,

[22] and Egwuatu [23] also recorded a significant decrease in urea levels in the 1st trimester. The progressive decrease in creatinine levels observed within the trimesters may be due to the increase in GFR, that occurs during pregnancy resulting in an increased clearance rate and decrease in serum concentration [24,25]. Edward *et al.*[26] reported that pregnancy increases the GFR to about $170ml/min/1.73m^3$ by 20 weeks and therefore increases the clearance of creatinine, urea and uric acid. Creatinine is not reabsorbed but rather secreted, any defect in its secretion leads to its accumulation in the body thereby increasing the serum level [27].

The progressive increase in sodium levels (although not statistically significant) may be attributed to the increase in the filtered load of sodium from non- pregnant level of 20,000mEq/day to approximately 30,000mEq/day during pregnancy to promote sodium retention for fetal and maternal use as reported by Monga, [28]. Although, there is no significant difference in sodium levels between the pregnant and non- pregnant women it is more retained and precisely regulated in the pregnant women than the non- pregnant control.

The findings in potassium levels in pregnant as compared to the non- pregnant subjects may be associated with the positive potassium balance and decreased excretion that occurs in pregnancy [29,30]. The decrease observed in the 3rd trimester (3.75±0.51) could be attributed to the fall in potassium levels to non- pregnant state at term [31].

It was observed that bicarbonate levels decreased from the 1st to the 3rd trimester with significant difference between the pregnant and non- pregnant subjects. The decrease in the arterial partial pressure of carbon dioxide ($PaCO_2$) due to an increase in the arterial partial pressure of oxygen (PaO_2) which occurs in normal pregnancy could be a possible explanation for the decrease in bicarbonate levels observed in the pregnant subject [32].

Serum chloride levels showed no significant difference between the pregnant and non- pregnant group and within the trimesters. This may likely be due to the fact that chloride metabolism is closely related to sodium and therefore influenced by similar factors [33]. There was a slight drop in chloride level in the 1st trimester with a return to the non- pregnant level thereafter. Newman [34] in his studies also found a slight drop during the 1st trimester with a return to non- pregnant level at term in normal pregnancy.

5. Conclusion

From the results of the above study it can be concluded that pregnancy is associated with physiological changes in renal function characterized by progressive decrease in creatinine and bicarbonate across all trimesters. Serum urea and chloride exhibit an earlier fall with a subsequent rise in the third trimester. Serum sodium rises progressively to reach a peak mean value in the third trimester.

6. Study Limitations/Constrains

The small sample size limit the projection of the results observed in this study to the population under study. It is therefore recommended that this study should be replicated with a much higher sample size.

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